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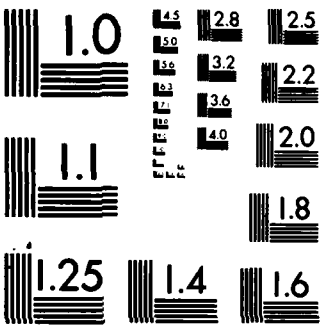

SVAS-PR-84-001
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Trans-1,4 polyisoprene	Gamma radiation	
Biocompatibility		

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The objective of this project was to develop a means of rejoining severed vessels (end-to-end anastomosis) without using sutures. Two essential elements in the concept, an instrument to evert the vessel and a biocompatible, low-temperature (130°F/54°C), heat-shrinkable sleeve were

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ENCLOSURE (1)

Block 20 Abstract continued

developed. The sleeve, which contracts to accomplish the anastomosis, was developed by crosslinking (with ionizing gamma radiation) synthetic trans-1,4 polyisoprene. The crosslinked polymer was subjected to an acute toxicity screening program and proved to be highly biocompatible. The sutureless anastomosis technique was tested in-vitro on freshly excised pig carotid arteries however, there was insufficient funding available to provide for an evaluation of the technique in laboratory animals.

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Introduction

Severed blood vessels are frequently encountered in penetrating wounds inflicted during combat, civil violence and accidents. When this type of injury is encountered near centers in which the skills and facilities are available, the blood vessels can be rejoined during vascular surgery with sutures. Under combat or emergency conditions, the prerequisite skills, facilities and time may not be available to prevent loss of limb or life.

At the present time vascular anastomosis is accomplished using a curved needle. The sutures must be placed precisely, piercing the adventitia (fibrous sheath) from the outside and the intima (elastic tissue layer) from the inside in a number of locations for proper vessel approximation (tissue aligned and in good contact). Either individual or continuous-running sutures are used.

Typically, for an artery with a 3mm lumen, approximately 20 stitches are taken around the circumference using a 6-0 (0.1mm diameter) thread. Usually, a single end-to-end anastomosis on vessels of this size cannot be performed in less than 20 minutes.

The greatest success is achieved when the anastomosis is performed in cases where a good collateral blood supply is available or in cases where loss of blood for moderate periods of time can be tolerated. If the intima is not approximated properly, vascular occlusion may occur with disastrous results.

The application of sutures on intracranial vessels is hampered by the following difficulties: differences in the structure of cerebral arteries as compared to extracerebral vessels with less adventitia and reduced media, the presence of many perforating branches precluding rotation, and the limited time of vessel occlusion.

The sutureless concept was conceived with the promise of avoiding some of these problems while providing potential benefits of high patency rate, virtual absence of post-operative bleeding and a faster procedure. Additionally, the skills required to apply this technique should be less than those required for suturing. Therefore, the work can be done at locations other than centers that specialize in vascular surgery.

Discussion

Figure 1 shows the steps involved in the sutureless anastomosis technique. Figure 1A shows the severed vessel which characteristically constricts and retracts because of the smooth muscular structure (media) within the vessel wall. In the first step temporary clips are applied to the transectioned vessel and the lumen irrigated with heparinized saline. The vessel diameter is sized, and ferrules are selected that approximately match the outside diameter of the vessel.

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Each vessel (Fig. 1B) section is then everted over a ferrule. An instrument to perform the vascular eversion has been developed. Everting fully opens the vessel for flow and ensures continuous intima contact, which is vital to prevent thrombosis after the anastomosis is completed.

In the next step, a sleeve, fabricated from a heat-shrinkable biocompatible thermoplastic, is placed on one section of the vessel. The two sections of the vessel are brought together and the sleeve is centered over the junction (Fig. 1C). The sleeve is heated with an instrument that provides a controlled warm airstream or jet of warm saline. Heat causes the sleeve to contract and assume the local contour of the everted vessel (Fig. 1D). In addition, the sleeve contracts 5 to 10 percent in length. This contraction ensures good contact of vascular intima.

In the completion sequence, the proximal clip is removed (Fig. 1D) and a hypodermic needle is inserted into the vessel lumen to relieve entrapped air. When a steady flow of blood through the hypodermic needle is achieved, the needle and distal clip is removed.

Vascular Everting Instrument

For the sutureless anastomosis technique to be a viable alternative to sutures, an effective means had to be developed to evert each severed vessel section over a ferrule. Two requirements essential for the everting instrument are (1) minimal damage and minimal displacement of endothelial cells lining the lumen and (2) flexibility for one instrument to evert vessels having a range of lumen diameters. Three devices were developed for bench studies of vascular eversion. The most successful of the three devices uses an iris-diaphragm mechanism to expand the leading ledge of the lumen and a balloon, inflated within the lumen, to accomplish the everting action. The iris-diaphragm mechanism uses two concentric rings. The outer ring is fixed and contains six wire expansion arms which are free to pivot. The inner ring contains six wire hoops. The expansion arms pass through the hoops and terminate with a short perpendicular segment. Rotation of the inner ring causes the arms to expand or contact radially depending on the direction of rotation. The iris-diaphragm mechanism is used in conjunction with a balloon syringe apparatus. This apparatus consist of a small balloon mounted to a hypodermic tube. The tube is centered within the lumen expansion arms. A syringe, connected to the hypodermic through a miniature check and control valve, is used to inflate/deflate the balloon with water. Freshly excised pig carotid arteries were successfully everted over thin-wall cylindrical ferrules using the everting apparatus configured for bench studies. On the basis of this success a prototype clinical configuration of the everter has been designed, built and tested in-vitro. Figure 2 is a photograph of the instrument. Figure 3 illustrates the means by which vascular eversion is accomplished. The sequence consist of (a) placing a properly sized ferrule on the artery, (b) inserting the deflated balloon of the everter into the vessel lumen, (c) inflating the balloon with the syringe, (d) expanding the leading edge of the lumen with the expander arms, (e) pulling the balloon and ferrule through the expanded lumen and (f) relaxing the lumen expander arms and deflating the balloon.

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Heat-Shrinkable Sleeve Development

The second essential element in the sutureless vascular anastomosis concept is the sleeve which contracts to bind the everted vascular sections together. Work began in this area with a literature study centered on identificaion of semicrystalline polymers that could undergo crosslinking (especially by ionizing radiation) and thereby attain elastic memory properties. Other requirements include biocompatibility, low-melting temperature (<60°C) and reasonable crystallinity.

Polyethylene oxide (PEO) was the first polymer selected for fabrication trials on the basis of preliminary radiation-chemistry experiments and the knowledge that the material is highly biocompatible. PEO was found to have two problems for this application: (1) the material would not conform to the extrusion die dimensions; (2) the material tended to become very slippery in water (hydrophilic). The first of these problems was solved through a trial and error adjustment of the PEO raw stock molecular weight. Experimentation demonstrated that uniform tubing could be extruded using PEO with a molecular weight of 200,000. Two approaches were taken in an attempt to overcome the tendency of PEO to swell in water; coating the sleeve with a waterproof material and grafting a monomer to the surface of the sleeve. Two monomers (styrene, ethylene) and two coatings (styrene/butadiene copolymer and silicone) were used but none provided the required degree of waterproof protection.

Work with PEO was abandoned and a review of literature reinitiated to find a suitable sleeve material.

This search lead to synthetic trans-1,4 polyisoprene (TPI). A reinforced form of this material has found use as a low-temperature moldable orthopedic material (Ref. 1).

Basic physical and radiation chemistry tests showed the material to be easily extrudable and crosslinkable with moderate radiation levels. Furthermore the materials is unaffected by water.

TPI was successfully extruded into small diameter tubes (4mm ID, 0.5mm wall thickness), and subsequently crosslinked with a 12 Mrad dose of gamma radiation. The TPI tubing is then heated to above its crystalline melt temperature (130°F/54°C) and its diameter is mechanically expanded 200 percent. Cooling "locks" the tubing in its expanded state. The tubing is then cut into short sections. When the processed sections or sleeves are reheated to 130°F/54°C they revert to within 5-10 percent of the original extruded diameter. The sleeves also contract some 5-10 percent in length.

The principal unknown property of TPI was its biocompatibility. Biocompatibility relates to the abiliity of the material to remain biologically inert during the implant period. It is frequently assessed in terms of the "toxicity" or lack of toxicity of the material. A primary acute

toxicity screening test was selected as the means of assessing the biocompatibility of TPI and the Materials Science Toxicology Laboratories at the University of Tennessee was asked to conduct the test.

The primary acute toxicity screening program included tests directly on TPI and tests on extracts of TPI. Table I lists the seven tests that were performed in the screening program. Reference 2 presents the test protocol. From the seven tests, fourteen biological responses (scored numerically) were used to calculate the Cummulative Toxicity Index (CTI). The CTI provides a quantitative measure of the toxic liability of the material. The CTI, theoretically ranges from a "low" of 0 to a "high" of 1500. In practice the screening program performed on numerous polymers has yielded CTI's ranging from a low of 30 to a high of 1050. Generally any material having a CTI less than 100 is considered to have a low toxic liability. Synthetic trans-1,4 polyisoprene received a CTI of 50 with no one test showing more than a minimum positive response. The material evaluation report (Reference 3) concluded that radiation crosslinked synthetic trans-1,4 polyisoprene has an extremely low potential toxic liability and is a good candidate material for implant.

In-Vitro Tests

Initial evaluation of the sutureless concept was conducted with in-vitro testing. The objective of the tests was to evaluate the structural integrity of the sutureless anastomosis technique. A secondary test objective was to evaluate the sutureless anastomosis procedure using the vascular everter and prototype ferrule and sleeve heating apparatus.

In-vitro testing of the sutureless anastomosis was performed on freshly excised pig carotid arteries. The arteries were transectioned and the end of each segment everted over a tapered polycarbonate ferrule. The two everted sections were abutted and centered within a processed TPI sleeve. Warm saline ($130^{o}F$) was used to contract the sleeve and bind the segments together. Visually the lumen was found fully patent throughout the length of the artery. An anastomosed artery was subjected to 1000 gm of axial tension and the joint remained intact.

Figure 4 shows the ferrules, sleeve and an anastomosed artery.

Summary

During the surge of battle casualties the prerequisite skills, facilities and time may not be available to perform end-to-end vascular anastomoses with sutures. A sutureless concept was proposed in which the proximal and distal portions of a severed vessel are everted over a ferrule and then the everted sections are bound together with a low-temperature, heat-shrinkable sleeve.

The objective of this project was to develop the materials, instruments and procedures necessary to implement the sutureless concept and to evaluate the technique on laboratory animals.

An instrument was successfully developed to effectively evert a severed vessel over a thin-wall ferrule. The instrument was bench tested using excised pig carotid arteries.

Inducing "elastic-memory" in a polymer by irradiation was selected as the most promising technology for developing the binding sleeve needed for the sutureless anastomosis concept. Two candidate polymers, polyethylene oxide (PEO) and synthetic trans-1,4 polyisoprene (TPI) received extensive radiation chemistry and sleeve processing experimentation.

PEO which satisfied the mechanical, biocompatibility and shrink-temperature requirements imposed by the anastomosis application could not be made hydrophobic. It tended to swell and become very slippery when placed in water.

Synthetic TPI met the mechanical and shrink-temperature requirements but had unknown biocompatibility.

Under subcontract, the Materials Science Toxicology Laboratories at the University of Tennessee performed an acute toxicity screen program on crosslinked TPI. The TPI was found to have an extremely low toxicity liability and was judged a good candidate material for implant.

The sutureless concept was successfully applied during in-vitro testing on excised pig carotid arteries.

Technical problems associated with development of the shrinkable sleeve resulted in insufficient funds available for an evaluation of the anastomosis technique on laboratory animals.

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Table I

Primary Acute Toxicity Screening Program

I. Test Directly on the Material

- Tissue Culture - Agar Overlay
- Rabbit Muscle Implant
- Hemolysis

II. Test on Extracts of the Material

- Tissue Culture-Agar Overlay
- Intracutaneous Injections in Rabbits
- Systemic Toxicity in Mice
- Cell Growth Inhibition

References

1. R. H. Jones and Y. K. Wei, Application of Trans-1,4 Polyisoprene in Orthopedic and Rehabilitation Medicine, J. Biomed. Mater. Res. Symposium, Vol. 1, pp 19-30 (1971)

2. J. Autian, Ph.D., Toxicological Evaluation of Biomaterials: Primary Acute Toxicity Screening Program, Artificial Organs, Vol. 1, pp 53-60 (1977)

3. J. Autian, Ph.D., Private correspondence, Report on Toxicity of Synthetic Trans-1,4 Polyisoprene under Project Number PT 0.1921, Materials Science Toxicology Laboratory, The University of Tennessee, dated February 1, 1984.

Fig. 1 Sutureless Vascular Anastomosis.

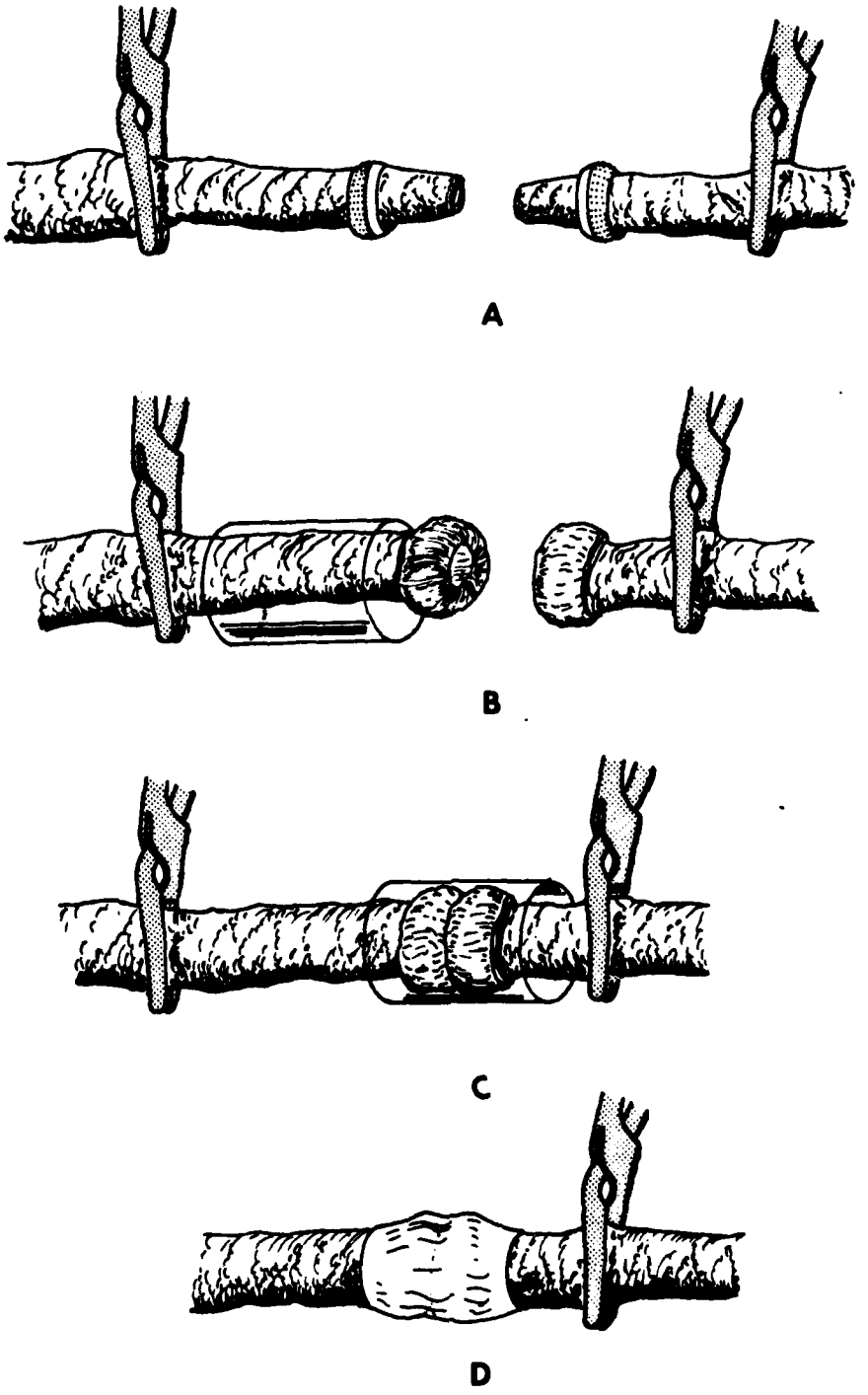
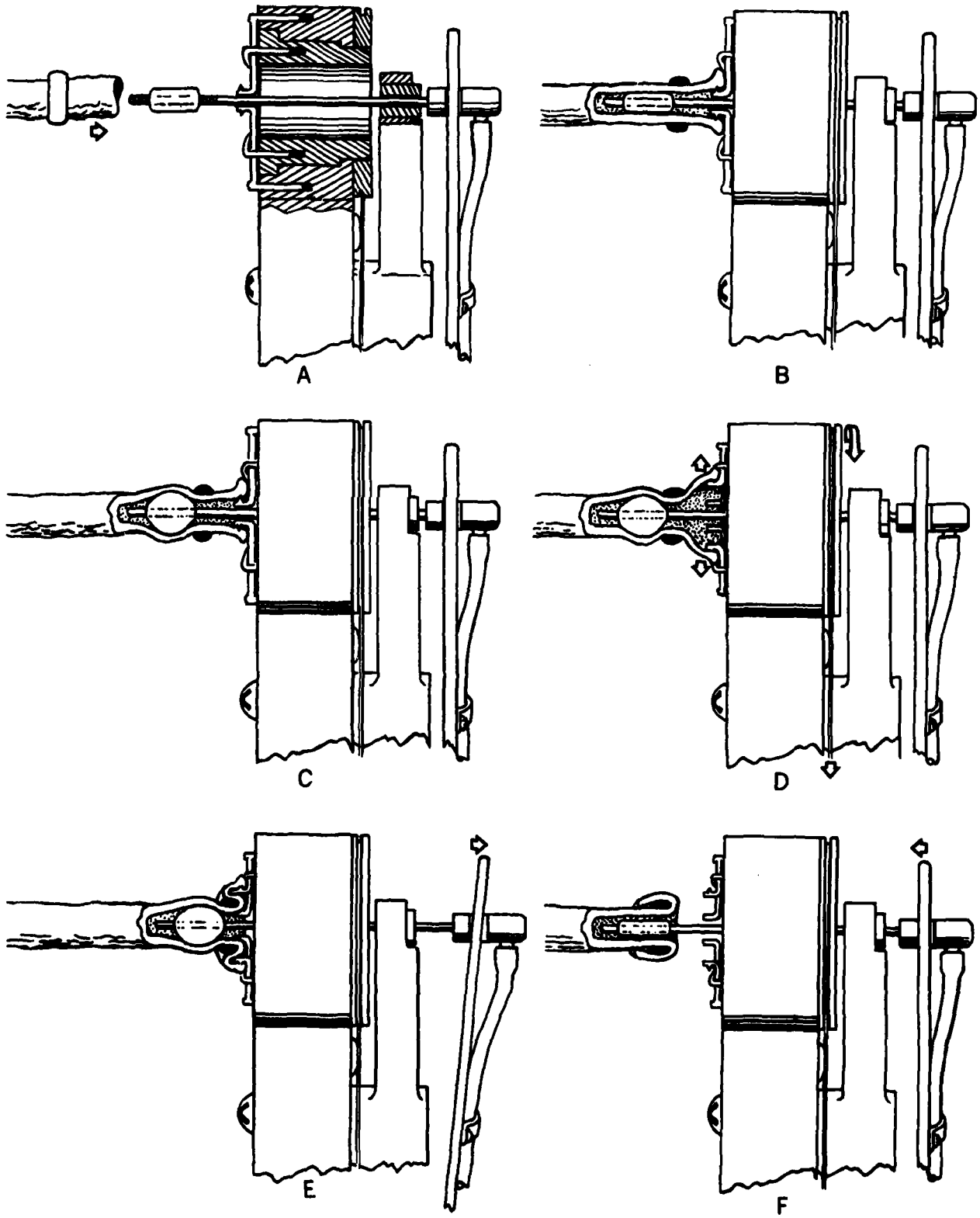


Figure 1

Figure 2



Operating sequence for vascular everter.

Figure 3

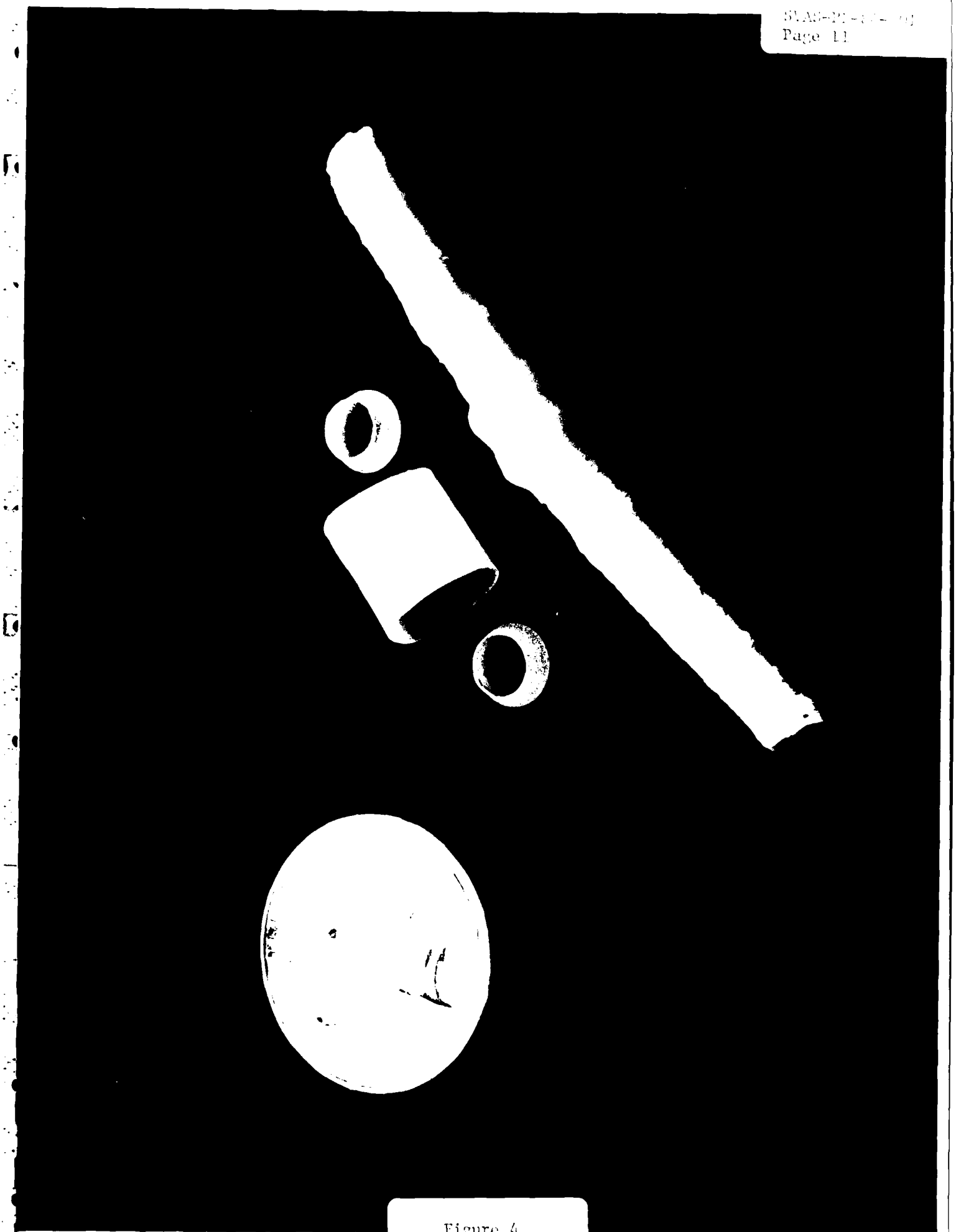


Figure 4